Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants would like to note that the present amendment is being submitted in compliance with "Amendments In A Revised Format Now Permitted", 1267 OG 4 (February 25, 2003). Pursuant to this notice, the requirements of 37 C.F.R. § 1.121 have been waived.

Applicants wish to thank the Examiner for the courtesy extended to applicants' undersigned representative during the telephone conference on November 8, 2002. The substance of the telephone conference is reflected below.

During the above-noted telephone conference, an objection was noted with regard to compliance with the requirements of 37 C.F.R. § 1.821 *et seq.* Specifically, the sequences of Figure 3 need to be identified by a sequence identification number. This objection to the specification has been overcome by the amendment to the description of the drawings so as to include sequence identification numbers therein. A revised sequence listing in paper form and computer readable form are also enclosed, along with a statement under 37 C.F.R. § 1.821. Applicants request entry of the revised sequence listing into the application.

The objection to the drawings is overcome by the accompanying submission of five (5) sheets of formal drawings.

Several amendments have been made to the specification to correct typographical errors. Apparently, during preparation of the specification, graphical symbols intended to appear as an "X" appeared instead as an "H". Thus, concentrations that should read as, e.g., 1 x 10^8 or 5X, instead appeared as 1H 10^8 or 5H, respectively. In addition, the designation of the additive "SSC" has been corrected from "SCC". The above amendments have corrected these typographical errors. No new matter has been entered by these amendments.

As discussed more fully below, the basis of all pending rejections is the need to specify parameters of hybridization and wash conditions. Because the PTO has indicated that such parameters are essential to specify the metes and bounds of the claim scope, and one or more parameters are incorporated by reference from a non-patent publication,

Sambrook et al., Molecular Cloning: A Laboratory Manual, (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY) (1989) ("Sambrook"), the "essential matter" must be copied from the non-patent publication into the specification. See MPEP § 608.01(p) (essential matter cannot be incorporated by reference from non-patent publications). Pursuant to MPEP 608.01(p), the undersigned hereby represents that the amendatory material consists of the same material incorporated by reference in the present application. See also In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). This is evident by the fact that Example 8 (page 25) of the present application describes the performance of a Southern hybridization assay and specifies certain variables of the hybridization and wash conditions, that Example 2 (page 23) specifies that the general molecular procedures employed in the provided Examples were performed using standard techniques as described in Sambrook, and that Sambrook is expressly incorporated by reference into the specification of the application (page 23). Because the Southern hybridization procedure was, as of 1997, a standard technique, the incorporation by reference of Sambrook included the incorporation by reference of the Southern hybridization protocol appearing at 9.31-9.57 of Sambrook (copy attached as Exhibit A). Thus, one of ordinary skill in the art would understand that parameters not provided by the Example 8 were intended to be supplied with reference to the standard techniques of Sambrook, which was incorporated by reference. As a result, no new matter has been introduced by the amendment to the paragraph appearing at page 25, lines 25-31.

The objection to claim 3 is overcome by the above amendment.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed in view of the above amendments and the following remarks.

Initially, applicants note that the comments concerning plant transformation was rendered moot by the cancellation of those claims without prejudice in the amendment filed March 18, 2002. Because claims directed to that subject matter have been withdrawn, applicants need not respond to the objections made by the PTO.

The basis of the rejection of claims 1 and 4-10 is that the specification "does not reasonably provide enablement for nucleic acids that hybridize under conditions of unspecified stringency to SEQ ID NO: 1" (office action at page 1). Applicants submit that

the above amendments overcome the basis of the rejection because the hybridization and wash conditions have been specified in sufficient detail to enable one of ordinary skill in the art to determine whether the complement of a given DNA molecule hybridizes to SEQ ID NO: 1 and whether such DNA molecule encodes a hypersensitive response elicitor.

For the reasons noted above, the incorporation by reference to Sambrook included matter which has now been introduced into the specification at page 25, lines 25-31. Such matter includes the hybridization solution used during the Southern hybridization procedure, which is 6X SSC, 5X Denhardt's reagent, and 0.5% SDS, and 100 μg/ml denatured fragmented salmon sperm DNA (see Exhibit A, Sambrook at 9.52). Example 8 specifies that the hybridization was carried out for 24 hours, either at 50°C (lower stringency) or 65°C (higher stringency) (see page 23). Washing was carried out under conditions to remove non-specifically bound probe, by two washes with either a solution of 2X SSC and 1.0% SDS at 65°C (higher stringency) or a solution of 2X SSC at 45°C (lower stringency), followed by repeated washes with 0.1X SSC until no radioactivity is detected in the wash solution (see id.). As for the wash conditions, Sambrook makes clear that repeated wash conditions are intended for various lengths of time. Specifically, Sambrook describes using initial washes (with a 2X SSC wash solution) that are short in duration, e.g., five minutes to fifteen minutes, followed by repeated washes (with a 0.1X SSC solution) that are longer in duration, e.g., 30 to 60 minutes (see Exhibit A, Sambrook at 9.54). Because one of ordinary skill in the art could, without undue experimentation, select varying wash times and continue the wash until no radioactivity (by the probe) is detected in the wash solution (indicating that only specifically hybridized probe remains bound to the isolated DNA attached to the membrane), the application fully enables one of ordinary skill in the art to perform the recited hybridization and wash conditions.

Applicants further submit that one of ordinary skill in the art would have been fully able to express the protein from a DNA molecule whose complement hybridizes to the DNA molecule of SEQ ID NO: 1 (see page 11, line 3 to page 14, line 19, describing recombinant techniques and protein purification procedures) and then determine whether the encoded protein does in fact elicit a hypersensitive response when infiltrated onto non-host plants. As demonstrated in Example 14 of the present application, the protein preparation can be infiltrated onto tobacco leaves to assay whether a hypersensitive response-like necrosis is induced (see page 29, lines 12-24 and Figure 5A).

For these reasons, applicants submit that the invention of claims 1 and 4-10 is fully enabled by the disclosure of the present application coupled with the knowledge in art at the time the present application was filed. Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of written descriptive support is respectfully traversed. The basis of this rejection is that the hybridization conditions are not recited with specificity and the activity of the protein is not recited. Applicants respectfully disagree.

For substantially the same reasons as noted above, one of ordinary skill in the art would fully recognize that applicants were in possession of isolated DNA molecules from other species of *Erwinia* that encode HrpW homologs. Applicants have identified a single species of *hrpW* by its nucleotide sequence (as well as the amino acid sequence of its encoded HrpW protein) and demonstrated, via the above-mentioned Southern hybridization procedures, that *hrpW* is indeed widespread among *Erwinia* pathogens (see Example 17 at pages 30-31).

In addition, the HrpW protein of SEQ ID NO: 2 is disclosed in the present application to share properties with other known hypersensitive response elicitors, including: characteristic amino acid composition such as being glycine rich and lacking in cysteine, heat-stability, low mobility in SDS-PAGE, and ability to elicit a hypersensitive response (see (page 9, lines 11-14 as previously amended; page 27, lines 19 to page 28, line 4; and page 29, lines 12-24; and page 31, line 3 to page 32, line 2). That these properties are shared by the art-recognized class of proteinaceous hypersensitive response elicitors is evident not only in the specification, but also in the prior art (see Bonas I, Bonas II, Preston, cited in and attached to response submitted on March 22, 2002).

Given the above demonstration by applicants, one of ordinary skill in the art would have understood that applicants were in possession of not just the isolated DNA molecule of SEQ ID NO: 1, but also the other isolated DNA molecules that applicants identified in the Southern hybridization experiments (by virtue of their hybridization to the *hrpW* probe). By virtue of their hybridization to the DNA molecule of SEQ ID NO: 1, one of ordinary skill in the art would have expected the proteins encoded by those isolated DNA molecules from other *Erwinia* species to similarly encode proteins capable of inducing a hypersensitive response-like necrosis in non-host plant tissues. Therefore, written descriptive support does indeed exist for the presently claimed invention.

For these reasons, the rejection of claims 1 and 4-10 for lack of written descriptive support is improper and should be withdrawn.

The rejection of claims 1-10 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments specifying parameters of the hybridization conditions and the wash conditions. Therefore, this rejection should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(a) as being anticipated by either Kim et al., "Hrp-secreted proteins and avirulence protein homologs of *Erwinia amylovora*," Phytopathol. 87:S52 (1997) ("Kim I") or Kim et al., "HrpW, A New Harpin of *Erwinia amylovora*, is a Member of a Family of Pectate Lyases," Phytopathol. 87:S52 (1997) ("Kim II") is respectfully traversed. (Again, the PTO has failed to cite whether Kim I or Kim II is being used in making the rejection.)

Kim I simply identifies the genomic location of the *Erwinia amylovora hrpW* gene as being between the *hrp* region and the *dsp* region. Kim I does not disclose how one of ordinary skill in the art would go about isolating the *hrpW* gene, let alone its nucleic acid sequence (e.g., SEQ ID No: 1), using the conditions recited in claim 1. Therefore, Kim I cannot have anticipated the presently claimed invention.

For reasons already of record in the response submitted on March 22, 2002 (and the Declaration of Steven V. Beer Under 37 C.F.R. § 1.132 that accompanied that response), Kim II is not available as prior art under 35 U.S.C. 102(a). See In re Katz, 687 F.2d 450 (Fed. Cir. 1982).

For all of the above reasons, the rejection of claims 1-10 over either Kim I or Kim II is improper and should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,850,015 to Bauer et al. ("Bauer '015 patent") is respectfully traversed. The PTO asserts that the *hrpN*$_{Ech}$ gene would hybridize to SEQ ID NO: 1 under the previously recited hybridization conditions. However, as acknowledged by the PTO during the above-referenced telephone interview, amendment of claim 1 to recite parameters of hybridization and wash conditions overcomes this rejection. Given the above amendments to specify the hybridization and wash conditions employed, applicants submit that the PTO's position is obviated because the Bauer '015 patent does not teach a DNA molecule as recited in claim 1. Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(b) as being anticipated by Wei et al., "Harpin, Elicitor of the Hypersensitive Response Produced by the Plant Pathogen *Erwinia amylovora*," Science 257:85-88 (1992) ("Wei") is respectfully traversed. The PTO cites to Wei for the proposition that the *hrpN* gene would hybridize to SEQ ID NO: 1 under the previously recited hybridization conditions. However, as acknowledged by the PTO during the above-referenced telephone interview, amendment of claim 1 to recite parameters of hybridization and wash conditions overcomes this rejection. Given the above amendments to specify the hybridization and wash conditions employed, applicants submit that the PTO's position is obviated because Wei does not teach a DNA molecule as recited in claim 1. Therefore, the rejection of claims 1-10 should be withdrawn.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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Date 4/17/03 | Wendy L. Barry